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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
HOLLERAN, ANNE L

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 09/24/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/806,301	MACINA, ROBERTO A.	
	Examiner	Art Unit	
	Anne Holleran	1642	

-- Th MAILING DATE of this communication appears n the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) *7-10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892) ✓
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) ✓ ✓
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *13,10,1* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1-6 (to the extent they read on methods of measuring levels of ESBPII polypeptides) in Paper No. 11, filed September 13, 2002, is acknowledged. The traversal is on the ground(s) that the restriction is improper because all of the invention groups relate to a single inventive concept. This is not found persuasive because, as set forth in the restriction requirement, group I is drawn to methods of measuring levels of ESBPII polypeptides, group II is drawn to methods of measuring ESBPII polynucleotides, group III is drawn to in vivo methods of imaging and detecting ESBPII polypeptide expressing tumors, and group IV is drawn to methods of treatment. Furthermore, an ESBPII polypeptide is known in the art as evidenced by teachings of WO97/34997 (cited in the IDS; published 25 September 1997), which teaches a sequence that is the same as that of SEQ ID NO: 2. Thus, ESBPII is not a special technical feature that unites all of the invention groups.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 1-10 are pending.

Claims 7-10, drawn to non-elected inventions, are withdrawn from consideration.

Claims 1-6, to the extent that they read on measuring levels of ESBPII polypeptides, are examined on the merits.

3. Claims 1-6 must be amended to reflect that the methods are drawn to measurement of ESBPII polypeptides.

4. The Office letter, mailed Dec. 3, 2002, is vacated, because the application does not contain figures, and the Figure 6 alluded to in the letter belongs to another application.

Information Disclosure Statement

5. In the IDS filed May 6, 2002, references AQ, AZ - BL, BN - BS, BU, BV and BX - CB were not considered, because copies of the references were not found with the file. Applicant is invited to send copies of these references for consideration.

Claim Rejections - 35 USC § 112

6. Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The basis for this rejection is that the term ESBPII is broadly defined in the specification so that the claims read on methods for diagnosing cancer by comparing levels of a protein that is not adequately described in the specification.

The specification defines ESBPII as referring to "among other things", a protein expressed by a gene comprising the polynucleotide of SEQ ID NO: 1 with the amino acid sequence of SEQ ID NO: 2. The specification fails to describe the "other things". Therefore, SEQ ID NO: 2 does not appear to be representative of the genus of polypeptides that are encompassed by the term ESBPII. A disclosure that does not adequately describe a product, in this case ESBPII, logically cannot adequately describe a method of using that product. In this

case, the specification does not describe the genus of polypeptides that constitute ESBPII that is required to practice the methods of claims 1-5. While the specification provides a structure of one member of the genus, the specification fails to provide a complete structure of any of the other polypeptides that belong to the genus of ESBPII proteins, nor does the specification provide any partial structures of such polypeptides, nor any physical or chemical characteristics of the polypeptides, nor any functional characteristics coupled with a known or disclosed correlation between structure and function. Furthermore, the specification fails to describe a representative number of species of the genus of ESBPII polypeptides, nor does is describe structural features common to the members of the genus. Since the specification fails to adequately describe the product, it also fails to adequately describe the claimed methods of using the product.

7. Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for diagnosis of breast cancer, does not reasonably provide enablement for diagnosis of prostate cancer or any gynecologic cancer; or for the diagnosis of metastasis, for the monitoring of change in stage, or the monitoring of onset of metastasis of prostate cancer or any gynecologic cancer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 1 is drawn to methods for diagnosing the presence of prostate cancer or any gynecologic cancer. Claim 2 is drawn to a method of diagnosing metastasis of prostate cancer or

of a gynecologic cancer. Claim 3 is drawn to a method of staging prostate cancer or a gynecologic cancer. Claim 4 is drawn to a method for monitoring prostate cancer or a gynecologic cancer for the onset of metastasis. Claim 5 is drawn to a method of monitoring a change in stage of a prostate cancer or a gynecologic cancer. Claim 6 (examined to the extent it reads on measuring levels of SEQ ID NO: 2), is dependent from claims 1, 2, 3, 4 or 5. As defined in the specification, a gynecologic cancer includes uterine, breast, endometrial or ovarian cancer. The methods of claims 2-5 are examined to the extent they comprise measuring levels of ESBPII polypeptides. The specification teaches that one example of an ESBPII polypeptide is a polypeptide having the sequence of SEQ ID NO: 2.

Factors to be considered in determining whether undue experimentation would be required to practice the full scope of the claimed inventions are: 1) quantity of experimentation necessary; 2) the amount of direction or guidance presented in the specification; 3) the presence or absence of working examples; 4) the nature of the invention; 5) the state of the prior art; 6) the relative skill of those in the art; 7) the predictability or unpredictability of the art; and 8) the breadth of the claims. See Ex parte Forman, 230 USPQ 546, BPAI, 1986.

The full scope of claim 1 is not enabled by the specification, because the specification fails to establish that measuring levels of a polypeptide having the sequence of SEQ ID NO: 2, or any other protein that is to be considered an ESBPII polypeptide, may be used for the diagnosis of prostate cancer or any gynecologic cancer other than breast cancer. The full scope of claims 2-6 are not enabled by the specification, because the specification fails to establish that measuring levels of a polypeptide having the sequence of SEQ ID NO: 2 may be used to diagnose metastasis of prostate cancer or a gynecologic cancer, to stage prostate cancer or a

gynecologic cancer, to monitor prostate cancer or a gynecologic cancer for onset of metastasis, or to monitor a change in stage of prostate cancer or of a gynecologic cancer. Furthermore, while the prior art teaches that the measurement of ESBPII polypeptides such as BU101 (see US 6,183,952) and mammoglobin (see US 6,566,072) can be used as the basis of the diagnosis of breast cancer, the prior art fails to teach that these results may be extrapolated to any gynecologic cancer or to prostate cancer. The data provided by the specification consists of Table 1 and Tables 2. Table 1 shows relative levels of mRNA in 12 normal tissues, and demonstrates that mRNA encoding ESBPII is highly expressed in normal breast, prostate and uterus. Table 2 shows mRNA levels in various cancer samples, cancer cell lines and compares the levels to non-cancerous adjacent or non-cancerous samples from another patient. The data of Table 2 does not appear to demonstrate that measuring levels of ESBPII would be diagnostic of cancer metastasis or cancer stage, because, for example in the endometrial samples, there is an increase in expression in 4 out of 11 samples, a decrease in expression in 6 out of 11 and no change in 1 out of 11 samples. For the case of prostate cancer, Table 2 shows that there is an increase in mRNA expression in 6 out of 13 samples, a decrease in 4 out of 13 samples and no change in 3 out of 13 samples. Furthermore, there is not data relating these changes with metastasis or stage of cancer. Thus, the specification presents an invitation to experiment to discover if an association exists between levels of ESBPII any gyncecologic cancer or prostate cancer, or an association between ESBPII levels and stage of either prostate cancer or gynecologic cancer.

Claims 1-6 are not enabled by the specification to the extent that the claims read on using measurements of protein levels as a basis for a method for diagnosis, staging or monitoring a change in cancer stage, because the data consists of mRNA measurements without any parallel

detection of protein. Even if the data of Table 2 could be used to establish that measurements of mRNA levels were diagnostic of prostate cancer or any gynecologic cancer; metastasis or a change in stage of prostate cancer or a gynecologic cancer, it is not predictable that measurements of the encoded protein also could be used as a basis for such diagnostic tests. Many proteins are regulated at the translational level rather than the transcriptional level. For instance, Shantz and Pegg (Int J of Biochem and Cell Biol., 1999, Vol. 31, pp. 107-122) teach that ornithine decarboxylase is highly regulated in the cell at the level of translation and that translation of ornithine decarboxylase mRNA is dependent on the secondary structure of the mRNA and the availability of eIF-4E, which mediates translation initiation. McClean and Hill (Eur J of Cancer, 1993, vol. 29A, pp.2243-2248) teach that p-glycoprotein can be overexpressed in CHO cells following exposure to radiation, without any concomitant overexpression of the p-glycoprotein mRNA. In addition, Fu et al (EMBO Journal, 1996, Vol. 15, pp. 4392-4401) teach that levels of p53 protein expression do not correlate with levels of p53 mRNA levels in blast cells taken from patients with acute myelogenous leukemia, said patients being without mutations in the p53 gene. Thus, steady state levels of protein are not necessarily correlated to steady state levels of mRNA, because of the homeostatic factors affecting transcription and translation.

Because the specification appears to be merely an invitation for further research to establish a correlation between levels of ESBPII and metastasis of, or stage of, or change in stage of prostate cancer or gynecologic cancer, further undue experimentation would be required for the practice of the claimed inventions. Further, because there is no data in the specification demonstrating a correlation between protein levels and prostate cancer or gynecologic cancer,

and because one cannot assume that a change in steady state levels of mRNA corresponds to a similar change in steady state levels of protein, the specification fails to establish that measurement of ESBPII protein levels could be used as the basis for the claimed methods.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

8. Claim 1 is rejected under 35 U.S.C. 102(e) as being anticipated by Watson (U.S. Patent 6,566,072; issued May 20, 2003; filing date Sep. 29, 1998).

Claim 1 is drawn to methods for diagnosing the presence of prostate or gynecologic cancer, comprising measuring levels of ESBPII in cells, tissues or bodily fluids; and comparing the measured levels of ESBPII with levels of ESBPII in cells, tissues or bodily fluids from a normal human control, wherein a change in measured levels of ESBPII in said patient versus normal human control is associated with the presence of prostate cancer or a gynecologic cancer. The specification defines gynecologic cancer to include breast cancer. Furthermore, the specification defines ESBPII broadly, so that proteins other than those having an amino acid sequence of SEQ ID NO: 2 are included within the scope of ESBPII.

Watson teaches a method for detecting the presence of breast cancer, comprising measuring levels of mammoglobin, a protein that is closely related to a protein having the amino acid sequence of SEQ ID NO: 2 (see claim 1; col. 23, line 3 – col. 24, line 31). Thus Watson teaches a method that is the same as that claimed.

9. Claims 1 and 6 are rejected under 35 U.S.C. 102(e) as being anticipated by Billing-Medel (U.S. Patent 6,183,952; issued Feb. 6, 2001; filing date Aug. 15, 1997).

Claims 1 and 6 are interpreted to read on methods for diagnosing the presence of prostate or gynecologic cancer, comprising measuring levels of ESBPII, wherein the ESBPII comprises the sequence of SEQ ID NO: 2, in cells, tissues or bodily fluids. The specification defines gynecologic cancer to include breast cancer.

Billing-Medel teaches methods for diagnosing the presence of breast cancer, comprising measuring a protein having the sequence of SEQ ID NO: 2 (referred to as BU101) (see col. 60, lines 7-9, col. 6, lines 12-35, col. 7, lines 48-61 and col. 64, lines 1-14). Thus, Billing-Medel teaches methods that are the same as that claimed.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Office should be directed to Anne Holleran, Ph.D. whose telephone number is (703) 308-8892. Examiner Holleran can normally be reached Monday through Friday, 9:30 am to 2:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D. can be reached at (703) 308-3995.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist at telephone number (703) 308-0196.

Anne L. Holleran
Patent Examiner
September 23, 2003

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